SPECIAL STATUS APPLICATION

Appl. No 10/659,413
Reply to Office Action mailed November 3, 2004
Amendment and Reply dated December 8, 2004

REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks. This Amendment and Reply to the Office Action mailed November 3, 2004 is being filed within the 3-month shortened statutory period. Applicants note that this application has been granted ***Special Status*** and respectfully request that the Examiner expedite his review of this Amendment and Reply.

Applicants' representative thanks Examiner Travers for the telephone call on October 14, 2004 concerning the election requirement for the subject application. A provisional election during the telephone conference was made without traverse to prosecute claims directed to compositions. Applicants affirm the provisional election and elect to prosecute claims directed to compositions. Claims withdrawn as directed to a non-elected invention, including claims 48-53, have been cancelled without prejudice to Applicants' ability to present and prosecute them in a related application.

Applicants note that the Examiner has renumbered the claims to correct the two claims numbered "39" presented in the Preliminary Amendment filed August 31, 2004. The second Claim 39 has been renumbered as Claim 40, and original Claims 40-52 have been renumbered as Claims 41-53.

Withdrawn claims 48-53 have been cancelled, as have claims 33, 35, 36, 38 and 43. These claims are canceled without prejudice. Independent claim 32 has been amended to specify that the EDTA salt(s) component in the antiseptic composition is at a concentration of at least 2.0% (w/v) and less than 15% (w/v), and to specify that the antiseptic composition is safe and biocompatible, at least in modest volumes, in a patient's bloodstream. The recited concentration range is described in the specification, as filed, at page 13, lines 6-14 and the biocompatibility feature of the applicants' claimed composition is described in the specification, as filed, at page 9, lines 5-13. Claim 54 has been added to specify an antiseptic composition *consisting essentially of* at least one EDTA salt and a solvent, the EDTA salt comprising tetra-sodium EDTA within a specified concentration range and the antiseptic composition having a bactericidal effect and having a specified pH. The compositions of claim 54 are described throughout applicants' specification, as filed.

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Claim 55 has been added to specify an antiseptic composition comprising a specified EDTA component having a specified concentration range, bactericidal effect and pH, wherein the composition additionally has an osmolarity within a specified range. This aspect of applicants' claimed invention is described in applicants' specification, as originally filed, at the paragraph spanning pages 17 and 18. Claim 56 has been added to specify a lock flush composition comprising an EDTA component at a specified concentration range and pH, and being safe and biocompatible for use in in-dwelling catheters, urinary catheters, nasal tubes and throat tubes. The compositions of claim 56 are described in applicants' specification, for example, at page 10, lines 16-29.

Claims 33, 35, 36, and 43 have been canceled. The subject matter of claim 38 has been recited in claim 37 and claim 38 has consequently been canceled. Claims 34, 37, 39, 40, 42 and 44-47 have been amended to multiple dependent format. Claims 32, 34, 37, 39-42, 44-47 and 54-56 are now pending in the application, with Claims 32, 54, 55 and 56 being in independent format.

Provisional Claim Rejections – 35 U.S.C. §101

Applicants note that Claims 32-48 are *provisionally* rejected under 35 U.S.C. § 101 as claiming the same invention as that of Claims 32-47 of co-pending Application No. 10/313,844. The Examiner stated that this is a *provisional* double patenting rejection since the potentially conflicting claims have not in fact been patented.

Following the Examiner's renumbering of claims and entry of the claim amendments presented herein, Claims 32, 34, 37, 39-42, 44-47 and 54-56 are pending in the subject application. Independent claims 32 (as amended herein), 54, 55 and 56 are recited above.

Applicants submitted a Second Preliminary Amendment in co-pending Application No. 10/313,844 on August 31, 2004. Following the Second Preliminary Amendment, Claims 7-17 and 21-24 are pending in Application No. 10/313,844, with Claims 7 and 21 being in independent format. Independent Claims 7 and 21 are shown below:

> 7. A method for disinfecting a conduit by contacting the conduit with a disinfectant solution consisting essentially of an ethylene diamine tetraacetic acid (EDTA) salt and a

solvent, wherein the EDTA salt is at a concentration sufficient to have a bactericidal effect over a broad spectrum of microbes and a destructive effect against a variety of yeasts, and wherein the EDTA salt comprises tetrasodium EDTA.

21. A method for disinfecting a catheter comprising: introducing a disinfectant solution into an interior lumen of the catheter, wherein the disinfectant solution consists essentially of an EDTA salt and a solvent, wherein the EDTA salt is at a concentration sufficient to have bactericidal effect over a broad spectrum of microbes and inhibitory effect against a variety of yeasts, and wherein the EDTA salt comprises tetrasodium EDTA; holding the disinfectant solution within the interior lumen for a selected period of time; and removing the disinfectant solution from the interior lumen.

Double patenting rejections based on the same invention being claimed in another co-pending application are only proper when the scope of the claimed inventions is identical. MPEP § 804. The inquiry is whether the same invention is being claimed twice. Independent Claims 32, 54, 55 and 56 of the subject application, as currently presented, are directed to *antiseptic compositions* and a *lock flush composition* comprising at least one EDTA salt and a solvent having concentration and pH values within specified ranges and having additional specified properties. Independent Claim 7 of co-pending Application No. 10/313,844 is directed to a *method for disinfecting a conduit* by contacting the conduit with a disinfectant solution; independent Claim 21 of co-pending Application No. 10/313,844 is directed to a *method for disinfecting a catheter* by introducing a disinfectant solution into an interior lumen of the catheter.

The independent claims in these co-pending applications are ***not*** co-extensive in scope. The claims are based on similar subject matter but they are not claiming the same subject matter, as prohibited by 35 U.S.C. §101. Based on the different scopes of independent claims 32, 54, 55 and 56 pending in the subject application and independent claims 7 and 21 of co-pending Application No. 10/313,844, applicants respectfully submit no basis for a statutory double patenting rejection exists. It is therefore urged that the provisional double patenting rejection of the pending claims under 35 U.S.C. §101 be withdrawn.

Claim Rejections – 35 U.S.C. §102(b) and §103 –

Merck Index and Kurginski

Merck Index

Claims 32-36, 39-41, and 45 are rejected under 35 U.S.C. §102(b) as being anticipated by Merck Index and under 35 U.S.C. §103 as being obvious in view of the Merck Index. These rejections are respectfully traversed, particularly in view of the amendments presented above and the following remarks.

The Examiner alleges that the Merck Index teaches tetra-sodium EDTA as an aqueous solution of 103 grams in 100 ml of water; yielding a 51.5% (w/v) solution, and that a 1% aqueous solution of this compound is taught as possessing a pH of 11. The Examiner observes that the cited Merck Index *fails* to teach an antibacterial use for the EDTA composition disclosed in the reference.

The Merck Index listing for tetra-sodium EDTA notes that the solubility of tetra-sodium EDTA in water is 103 g/100 ml, which gives rise to the Examiner's calculation of a 51.5 % solution (w/v). In addition, the listing notes that the pH of a 1% tetra-sodium EDTA solution has a pH of 11.3. These are the only EDTA concentrations cited by the Merck index listing for tetra-sodium EDTA. Applicants disagree that the listing of these EDTA properties in the Merck Index constitutes a "teaching" of EDTA solutions having the specified concentrations. Nonetheless, applicant's claims have been amended to recite antiseptic compositions that are clearly outside the range of tetra-sodium EDTA concentrations cited in the Merck index to expedite prosecution and allowance of the pending claims. Applicants' pending claims recite antiseptic compositions and lock flush compositions comprising at least one salt of EDTA, wherein the EDTA salt comprises tetra-sodium EDTA and is at a concentration of *at least 2.0% (w/v) and less than 15% (w/v)*. It is urged that applicants' claimed solutions are ***not*** anticipated by the Merck Index listing.

Applicants note that the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. The Merck Index recites various properties of tetra-sodium EDTA, including its solubility in water (51.5%) and the pH of a 1% solution. It is urged

that the Examiner has not and cannot make a showing of why one of ordinary skill in the art at the time the invention was made would have been motivated, knowing the solubility of tetra-sodium EDTA in water and the pH of a 1% solution of tetra-sodium EDTA, to make the applicants' claimed antiseptic and lock flush compositions. More specifically, it is urged that one of ordinary skill in the art, without knowledge of applicants' work, would *not* have been motivated, knowing the solubility and pH properties of tetra-sodium EDTA as recited in the Merck Index listing, to make or use compositions comprising at least one salt of EDTA and a solvent, wherein the EDTA salt comprises tetra-sodium EDTA and is at a concentration of *at least 2.0% (w/v)* and *less than 15% (w/v)*, the antiseptic composition having a bactericidal effect over a broad spectrum of microbes, having a pH of at least 9.5, and being safe and biocompatible, at least in modest volumes, in a patient's bloodstream.

Applicants do not concede or concur in the Examiner's statement that *any* uses or functions of the claimed antiseptic compositions inherently reside in the composition(s) disclosed in the Merck Index but believe that any inherency argument is rendered moot in view of the above amendments and remarks.

Kurginski (DE 1044363)

Claims 32-43 and 45 are rejected under 35 U.S.C. §102(b) as being anticipated by and under 35 U.S.C. §103 as being obvious in view of *Kurginski* (DE 1944363). The Examiner alleges that *Kurginski* teaches an aqueous solution (ca. 0.25% to 15%) of tetra-sodium EDTA, in combination with alcohol, at a preferred pH of 10-11. The Examiner further states that *Kurginski* exemplifies an antibacterial use for Applicants' claimed EDTA/alcohol composition, wherein no ethanol is present, although an antibacterial use is taught for the compositions globally. This rejection is respectfully traversed, particularly in view of the claim amendments presented above and the following remarks.

The Delphion record for *Kurginski* (DE 1944363) indicates that there are several patent family members related to the German (DE 1944363) *Kurginski* patent publication, including the English-language British patent specification GB 1279148A. The Delphion record, as well as a copy of British Patent specification 1 279 148 are attached as Exhibit A for the Examiner's

reference. The Declaration of Dr. Stephen Olmstead is attached as Exhibit B[1], verifying that the German language *Kurginski* application is the same as the English language *Kurginski* application. We refer to the British *Kurginski* Patent specification 1 279 148 in our remarks below.

Kurginski discloses an industrial cleaning solution for use in the sanitary maintenance of toilet facilities. The aqueous cleaning composition has a pH of from 7 – 12 and comprises a chelating agent (in the amount of 0.25-15 parts); a loweralkanol (in the amount of 1-5 parts); an alkanolamine (in the amount of 0.8-6 parts); and a mixture of two or more different loweralkyl ether alcohols (in the amount of 1-5 parts). Additional components such as surfactants, foaming or de-foaming agents, germicides and the like may also be used. EDTA is among the chelating agents listed as suitable, and tetrasodium EDTA is among the ingredients of a preferred composition described at the paragraph spanning Cols. 3 and 4, as well as in the composition described in Example 1.

Applicants' independent claim 32 has been amended to provide that the claimed antiseptic composition, in addition to having the specified composition, pH and bactericidal effect, is safe and biocompatible, at least in modest volumes, in a patient's bloodstream. Independent claim 55 recites a specified osmolarity range for the antiseptic composition, and independent claim 56 specifies that the claimed lock flush composition is safe and biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes. It is urged that the *Kurginski* toilet cleaning solutions, comprising a loweralkanol (in the amount of 1-5 parts), an alkanolamine (in the amount of 0.8-6 parts), and a mixture of two or more different loweralkyl ether alcohols (in the amount of 1-5 parts) in addition to a chelating agent and optional surfactants, foaming agents, de-foaming agents, germicides, and the like, would *not* be safe and biocompatible, at least in modest volumes, in a patient's bloodstream, nor would they be safe and biocompatible for use in in-dwelling access catheters, urinary catheters, nasal tubes and throat tubes. Methanol, isomeric butanol, ether alcohols, alkylbenzene sulfonates, alkylated,

[1] Dr. Olmstead's Declaration is presently unsigned. He has reviewed the German and English language specifications and verifies they are substantially the same. Dr. Olmstead is presently out of the country and unavailable to sign the Declaration. We will submit a signed Declaration to the Examiner during the week of December 13, 2004.

sulfonated diphenyl oxides, *o*-phenylphenol, 4-chloro-2-cyclopentylphenol, and the like are cited as desirable components of the *Kurginski* cleaning solutions. The use of many of these constituents, alone and in combination with other recited constituents, clearly indicate that the *Kurginski* cleaning solutions are not intended for use in contact with or in close proximity to a patient's blood stream. The applicants' claimed antiseptic and lock flush compositions are not taught by, nor are they rendered obvious in view of the teachings of *Kurginski*.

It is urged that the Examiner's statements with regard to *Kurginski* teaching compositions containing alcohols are rendered moot by the above amendments and remarks. Applicants' pending claims differ from the disclosures of the *Kurginski* reference by far more than the intended application for the compositions. Applicants again do *not* concur with or acquiesce in the Examiner's statement that antimicrobial benefits would inherently reside in the prior art compositions disclosed by *Kurginski*.

The Examiner makes reference to the "Kurginski teaching of broad spectrum anti-microbial activity." Applicants find no such teaching in *Kurginski* and, in fact, note that *Kurginski* states at Col. 3, lines 74-76 that, when desired, a germicide can be added to a composition of the invention to disinfect or sterilize surfaces. Applicants believe that this statement would indicate to one of ordinary skill in the art that the compositions of *Kurginski* would ***not***, in fact, have germicidal properties and that if germicidal properties were desired, a germicide must be added. There is no indication or suggestion in *Kurginski* that a combination of fewer than all of the listed components, or a combination of one of the listed components with other components, would be useful or efficacious for any purpose, nor would there be any motivation to use fewer than all of the listed components. There would be no motivation to remove components that are toxic, for example, from the *Kurginski* composition to provide a resulting composition comprising fewer than all of the listed components that is safe and biocompatible, at least in modest volumes, in a patient's bloodstream. There would be no expectation, based on the teachings of *Kurginski*, that any such composition comprising fewer than all of the listed components, would have any bactericidal efficacy or other useful property.

Applicants further note that *Kurginski* states that when employing an antimicrobial substance, the pH of the composition becomes critical and *may not go above a pH of about 7 to*

8. This is clearly outside the pH range of applicants' claimed antiseptic compositions. *Kurginski* teaches, furthermore, that any given combination of components must be tested for germicidal activity and efficacy after the combination is prepared and that the germicidal activity of the composition is not predictable based on the known properties of the components. [See Col. 3, lines 75-98.] This teaching would motivate one of ordinary skill in the art to add various known germicidal components to the *Kurginski* solution, adjust the pH of the combination to a generally lower pH, and test the combination for germicidal activity. It is urged that the teachings of *Kurginski*, in fact, teach strongly away from the applicants' claimed compositions and that the Examiner has not, and cannot, make a showing of why one of ordinary skill in the art at the time the invention was made would have been motivated, knowing the teachings of *Kurginski*, to make the applicants' claimed antiseptic compositions and lock flush solution. Applicants' pending claims are *not* anticipated by nor rendered obvious in view of *Kurginski*. The rejections of the pending claims in view of *Kurginski* must be withdrawn.

Claim Rejections - 35 U.S.C. §103

Merck Index and Cherepanov et al. in view of Remington's Pharmaceutical Sciences

Claims 44, and 46-48 stand rejected under 35 U.S.C. §103 as being unpatentable over the Merck Index and *Cherepanov et al.*, in view of *Remington's Phatrmaceutical Sciences*. This rejection is respectfully traversed, particularly in view of the above amendments and the following remarks.

The Merck Index listing for tetra-sodium EDTA is described above. The *Cherepanov et al.* abstract discloses the intravenous injection of sheep with EDTA Na salt. The Examiner provided a copy of the *Cherepanov et al.* abstract and did not provide a copy of the *Cherepanov et al.* article upon which the abstract is based. It is the *Cherepanov et al.* abstract, therefore, and not the article, that forms the basis for the rejection. The *Cherepanov et al.* abstract discloses the use of "EDTA Na salt," which is *not* a teaching of the intravenous administration of a solution comprising *tetra-sodium* EDTA. Applicants do not discern any indication in the *Cherepanov et al.* abstract of which EDTA sodium salt (di, tri-, and/or tetra) was used for the intravenous injection. As noted in applicants' specification, when used in a clinical setting, or in a

composition that interacts with humans or animals, EDTA compositions are generally adjusted to a physiological, or neutral, pH range. Without any specific disclosure that *Cherepanov et al.* are using the *tetra-sodium* salt of EDTA for intravenous injections, it is therefore urged that one of ordinary skill in the art would presume *Cherepanov et al.* are using an EDTA solution that has a generally physiological pH for injection. At generally physiological pH, EDTA solutions comprise primarily tri-sodium EDTA, with a lesser proportion of the di-sodium salt. There is no indication or suggestion to use tetra-sodium EDTA, nor is there any motivation to do so.

Remington's Pharmaceutical Sciences teaches hypodermic syringes as conventionally being 50 ml or less. The Examiner further observes that *Remington's Pharmaceutical Sciences* warns against injection of solutions containing pyrogens and teaches saline solutions as ideal for injections. Applicants agree that hypodermic syringes are well known and that pyrogen-free compositions and saline solutions are conventionally used for compositions intended for human or animal therapeutic or diagnostic injection.

The Examiner argues that a skilled artisan would have been motivated to provide a syringe filled with applicants' claimed EDTA solution(s) in a pyrogen-free form, in a saline carrier, in view of the *Cherepanov et al.* teaching of intravenous injection of a sodium EDTA solution and *Remington's* teaching of injectable pyrogen-free saline solutions. Applicants disagree and submit that the teachings of the *Cherepanov et al.* abstract and the *Remington's* reference do not overcome the deficiencies of the Merck Index listing for tetra-sodium EDTA with respect to applicants' claimed antiseptic compositions. There is no suggestion or motivation, in view of any combination of teachings of the references cited for rejection, for a person of ordinary skill in the art to make or use applicants' claimed tetra-sodium EDTA compositions having the specified concentration ranges, pH properties and safety profiles. There is no suggestion anywhere in the prior art cited by the Examiner to formulate such antiseptic compositions to provide compositions that are safe and biocompatible, at least in modest volumes, in a patient's bloodstream. There is no motivation anywhere in the prior art cited by the Examiner to provide applicants' claimed antiseptic compositions in a pre-filled syringe or a single-use vial or in a dry or partially hydrated formulation suitable for reconstitution with a solvent. Neither the claimed compositions nor any utility for the claimed compositions has been

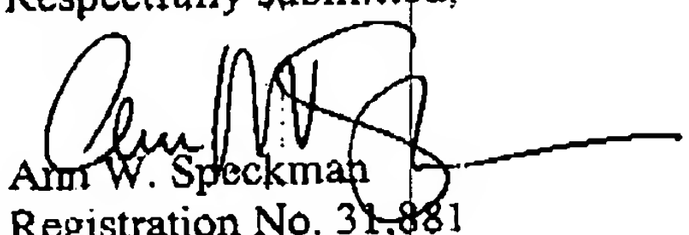
previously recognized and there has therefore been no motivation whatsoever to formulate and package the applicants' claimed compositions, as specified in applicants' pending claims.

It is urged that no combination of teachings of the Merck Index and *Cherepanov et al,* in view of *Remington's Pharmaceutical Sciences* would render applicants' pending claims obvious to one of skill in the art, and withdrawal of the present rejection under 35 U.S.C. §103 is thus required.

Conclusion

Early reconsideration and allowance of applicants' pending claims is respectfully requested.

Respectfully submitted,



Ann W. Speckman
Registration No. 31,881

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SPECKMAN LAW GROUP PLLC

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